DATA EVALUATION RECORD

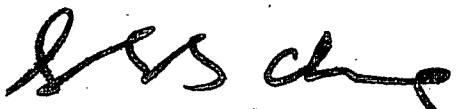
SLUGKIL MP (FENAEDTA)

STUDY TYPE: ACUTE ORAL TOXICITY - RAT (870.1100)
MRID 47942507

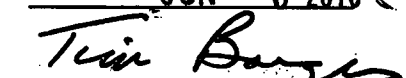
Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 10-004

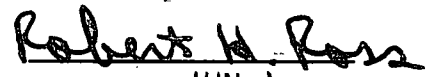
Primary Reviewer:
Susan Chang, M.S.

Signature: 
Date: JUN 10 2010

Secondary Reviewers:
H. Tim Borges, Ph.D., M.T.(A.S.C.P.), D.A.B.T.

Signature: 
Date: JUN 10 2010

Robert H. Ross, M.S., Group Leader

Signature: 
Date: JUN 10 2010

Quality Assurance:
Eric Lewis, M.S.

Signature: 
Date: JUN 10 2010

Disclaimer

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Oak Ridge National Laboratory managed and operated by UT-Battelle, LC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA EVALUATION RECORD

EPA Secondary Reviewer:

STUDY TYPE:	Acute Oral Toxicity - Rats (OPPTS 870.1100)
MRID NO:	47942507
DP BARCODE NO:	DP 373965
DECISION NO:	425379
SUBMISSION NO:	866101
TEST MATERIAL:	FeNaEDTA (EPA Reg. No. 67702-GR, ethylenediaminetetraacetic acid iron (III) sodium salt, containing 69.9% EDTA, a.i.)
PROJECT NO:	21617 (Report No.)
SPONSOR:	Neudorff GmbH KG, Postfach 1209, An der Mühle 3, D-31860 Emmerthal, Germany
TESTING FACILITY:	LPT Laboratory of Pharmacology and Toxicology GmbH & Co. KG, P.O. Box 920461, D-21134 Hamburg, Germany
TITLE OF REPORT:	Acute Oral Toxicity
AUTHOR:	Dr. Phil. J. Leuschner
STUDY COMPLETED:	September 17, 2007
GOOD LABORATORY PRACTICE:	GLP Compliant, according to EC method B.1 tris (2004/73/EC) and OECD guideline 423 (ATC method)
CONCLUSION:	The oral LD_{50} for female rats was greater than 2000 mg/kg.
CLASSIFICATION:	ACCEPTABLE -- TOXICITY CATEGORY III

I. STUDY DESIGN:

1. **Test Material**: FeNaEDTA - ethylenediaminetetraacetic acid iron (III) sodium salt, Batch No. 080 507, containing 69.9% EDTA, a.i.

2. **Test Animals:** Six female CD/Crl:CD(SD) rats were received from Charles River Laboratories, Research Models and Services, Germany GmbH, Sandhofer Weg 7, 97633 Sulzfeld, Germany and weighed 177-183 g on the day of dosing. The young adult animals, 7 weeks old, were housed in groups of three animals in Makrolon cages (type III). The animals were fed commercial diet, ssniff® R/M-H V1534 (ssniff Spezialdiäten GmbH, 59494 Soest, Germany). Drinking water in bottles was available *ad libitum*. The environmental conditions of the animal room were as follows: temperature, 22±3°C; relative humidity, 55±15%; and photoperiod, 12 hour light/dark cycle. The air changes per hour were not reported.

3. **Methods:** Rats were identified by colored marks and cage label: Nos. 1f to 6f and were acclimated for at least 5 days and fasted approximately 16 hours prior to dosing. The test material (2000 mg/kg body weight, suspended in 0.8% aqueous hydroxypropylmethyl-cellulose gel) was dosed by gavage (Table 1). Body weight was recorded prior to dosing, and on test days 8 and 15. The test animals were observed for clinical signs of toxicity before and immediately after treatment, at 5, 15, 30, and 60 minutes, and 3, 6, and 24 hours post-dosing and at least daily for 14 days. Mortality was checked at least once daily. All animals were necropsied at the end of the study.

II. RESULTS:

1. **Mortality:** All rats survived the study.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg)	Males	Females	Combined
2000	-	0/3	-
2000	-	0/3	-

Data taken from Table 1, p. 21, MRID 47942507.

2. **Body Weight:** All rats gained weight during the study.

3. **Clinical Observations:** No signs of toxicity were revealed.

4. **Gross Necropsy:** No pathological findings were noted at necropsy.

III. DISCUSSION:

The oral LD_{50} for female rats was greater than 2000 mg/kg. This places FeNaEDTA in TOXICITY CATEGORY III. The packet classification is **ACCEPTABLE.**

DATA EVALUATION RECORD

SLUGKIL MP (FENAEDTA)

STUDY TYPE: ACUTE DERMAL TOXICITY - RAT (870.1200)
MRID 47942508

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
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Prepared by
Toxicology and Hazard Assessment Group
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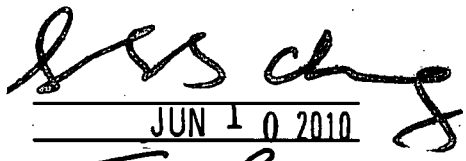
Oak Ridge, TN 37831
Task Order No. 10-004

Primary Reviewer:
Susan Chang, M.S.

Signature: 
Date: JUN 10 2010

Secondary Reviewers:
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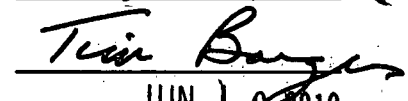
Signature: 
Date: JUN 10 2010

Robert H. Ross, M.S., Group Leader

Signature: 
Date: JUN 10 2010

Quality Assurance:
Eric Lewis, M.S.

Signature: 
Date: JUN 10 2010

Disclaimer

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Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA EVALUATION RECORD

EPA Secondary Reviewer:

STUDY TYPE:	Acute Dermal Toxicity - Rats (OPPTS 870.1200)
MRID NO:	47942508
DP BARCODE NO:	DP 373965
DECISION NO:	425379
SUBMISSION NO:	866101
TEST MATERIAL:	FeNaEDTA (EPA Reg. No. 67702-GR, ethylenediaminetetraacetic acid iron (III) sodium salt, containing 69.9% EDTA, a.i.)
PROJECT NO:	21618 (Report No.)
SPONSOR:	Neudorff GmbH KG, Postfach 1209, An der Mühle 3, D-31860 Emmerthal, Germany
TESTING FACILITY:	LPT Laboratory of Pharmacology and Toxicology GmbH & Co. KG, P.O. Box 920461, D-21134 Hamburg, Germany
TITLE OF REPORT:	Acute Dermal Toxicity Study
AUTHOR:	Dr. Phil. J. Leuschner
STUDY COMPLETED:	September 17, 2007
GOOD LABORATORY PRACTICE:	GLP Compliant, according to EC method B.3 (92/69/EEC) and OECD guideline 402
CONCLUSION:	The dermal LD_{50} for males, females, and combined sexes was greater than 2000 mg/kg.
CLASSIFICATION:	ACCEPTABLE -- TOXICITY CATEGORY III

I. STUDY DESIGN:

1. **Test Material:** FeNaEDTA - ethylenediaminetetraacetic acid iron (III) sodium salt, Batch No. 080 507, containing 69.9% EDTA, a.i.

2. **Test Animals:** Five male and five female CD/Crl:CD(SD) rats were received from Charles River Laboratories, Research Models and Services, Germany GmbH, Sandhofer Weg 7, 97633 Sulzfeld, Germany and weighed 222-253 g (males) and 207-230 g (females) on the day of treatment. The young adult animals, 51-65 days old, were housed individually in Makrolon cages (type III). The animals were fed commercial diet, ssniff® R/M-H V1534 (ssniff Spezialdiäten GmbH, 59494 Soest, Germany). Drinking water in bottles was available *ad libitum*. The environmental conditions of the animal room were as follows: temperature, 22±3°C; relative humidity, 55±15%; and photoperiod, 12 hour light/dark cycle. The air changes per hour were not reported.

3. **Methods:** Rats were identified by colored marks and cage label: Male – Nos. 1m to 5m; Female – Nos. 6f to 10f. The rats were acclimated for at least 5 days. The test material (2000 mg/kg body weight), suspended in water, was applied to 8 layers of gauze and placed over a 5 cm x 6 cm area (approximately 10% of body surface) of the shaved dorsal trunk. The gauze was covered with plastic sheet and secured with adhesive plaster. The coverings were removed after 24 hours. Body weight was recorded prior to dosing, and on test days 8 and 15. The test animals were observed for clinical signs of toxicity before and immediately after treatment, at 5, 15, 30, and 60 minutes, and at 3, 6, and 24 hours post-treatment, and at least daily for 14 days. The skin was observed for erythema, edema, and necrosis daily. Mortality was checked at least once daily. All animals were necropsied at the end of the study.

II. RESULTS:

1. **Mortality:** All rats survived the study.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg)	Males	Females	Combined
2000	0/5	0/5	0/10

Data taken from Table 1, p. 22, MRID 47942508.

2. **Clinical Observations:** No skin reactions or clinical signs of toxicity were noted throughout the study.

3. **Body Weight:** All rats gained weight during the study.

4. **Gross Necropsy:** No pathological findings were noted at necropsy.

III. DISCUSSION:

The acute dermal LD_{50} for males, females, and combined sexes was greater than 2000 mg/kg. This places FeNaEDTA in TOXICITY CATEGORY III. The packet classification is **ACCEPTABLE.**

DATA EVALUATION RECORD

SLUGKIL MP (FENAEDTA)

STUDY TYPE: PRIMARY EYE IRRITATION - RABBIT (870.2400)
MRID 47942509

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
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Prepared by
Toxicology and Hazard Assessment Group
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Oak Ridge, TN 37831
Task Order No. 10-004

Primary Reviewer:
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Date: JUN 10 2010

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date: JUN 10 2010

Quality Assurance:
Eric Lewis, M.S.

Signature: Eric B. Lewis
Date: JUN 10 2010

Disclaimer

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Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA EVALUATION RECORD

EPA Secondary Reviewer:

STUDY TYPE:	Acute Eye Irritation - Rabbits (OPPTS 870.2400)
MRID NO:	47942509
DP BARCODE NO:	DP 373965
DECISION NO:	425379
SUBMISSION NO:	866101
TEST MATERIAL:	FeNaEDTA (EPA Reg. No. 67702-GR, ethylenediaminetetraacetic acid iron (III) sodium salt, containing 69.9% EDTA, a.i.)
PROJECT NO:	21621 (Report No.)
SPONSOR:	Neudorff GmbH KG, Postfach 1209, An der Mühle 3, D-31860 Emmerthal, Germany
TESTING FACILITY:	LPT Laboratory of Pharmacology and Toxicology GmbH & Co. KG, P.O. Box 920461, D-21134 Hamburg, Germany
TITLE OF REPORT:	Primary Eye Irritation
AUTHOR:	Dr. J. Leuschner
STUDY COMPLETED:	August 7, 2007
GOOD LABORATORY PRACTICE:	GLP Compliant, according to EC method B.5. (2004/73/EC) and OECD guideline 405
CONCLUSION:	Corneal opacity was noted on 1/3 rabbits at 24 hours after test material instillation with resolution by day 7. Iritis was not noted on any rabbit during the study. No positive conjunctival irritation was noted on any rabbit. Some hyperemic blood vessels were noted on animal No. 1 at 60 minutes after test material instillation, on animal No. 2 at 60 minutes through 48 hours, and on animal No. 3 at 24 hours through day 4. The maximum average score was 3.0 at 24, 48, and 72 hours after test material instillation under the assumption that the area of opacity was 1/4 and discharge scores were 0. FeNaEDTA was mildly irritating.
CLASSIFICATION:	ACCEPTABLE – TOXICITY CATEGORY III

I. STUDY DESIGN:

1. **Test Material:** FeNaEDTA - ethylenediaminetetraacetic acid iron (III) sodium salt, Batch No. 080 507, containing 69.9% EDTA, a.i.

2. **Test Animals:** Three male young adult Himalayan rabbits were received from LPT Laboratory of Pharmacology and Toxicology GmbH & Co. KG, Branch Löhndorf, 24601 Löhndorf/Post Wankendorf, Germany. The animals were housed individually in cages. The animals were fed commercial diet, ssniff® K-H V2333 (ssniff Spezialdiäten GmbH, 59494 Soest, Germany). Tap water was available *ad libitum*. The environmental conditions of the animal room were as follows: temperature, 20±3°C; relative humidity, 30-70%; air changes, 60 per hour; and photoperiod, 12 hour light/dark cycle.

3. **Methods:** Rabbits were tattooed (Nos. 1, 2, and 3) and acclimated for at least 20 days. The test material (100 mg/eye/animal) was applied into the conjunctival sac of the right eye, and the eye held closed for approximately one second. The left eye served as control. One hour after treatment the eye was rinsed with 20 mL sodium chloride solution. The eyes were examined and scored 1, 24, 48 and 72 hours and at 4 and 7 days after test material instillation.

II. RESULTS:

1. **Mortality:** All rabbits survived the study.

2. **Ocular Lesions:** Corneal opacity was noted on 1/3 rabbits at 24 hours after test material instillation with resolution by day 7 (Table 1). Iritis was not noted on any rabbit during the study (Table 2). No positive conjunctival irritation (score ≥ 2) was noted on any rabbit. Some hyperemic blood vessels were noted on animal No. 1 at 60 minutes after test material instillation, on animal No. 2 at 60 minutes through 48 hours, and on animal No. 3 at 24 hours through day 4. The maximum average score was 3.0 at 24, 48, and 72 hours after test material instillation under the assumption that the area of opacity was 1/4 and discharge scores were 0 (Table 3).

TABLE 1. Individual Male (M) and Female (F) Eye Scores w/ Time: Cornea (A=Density of Opacity, B=Area of Opacity)

Animal No.	1 hour		24 hours		48 hours		72 hours		4 days		5 days		6 days		7 days	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
1	0	-[a]	0	-	0	-	0	-	0	-	0	-	0	-	0	-
2	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-
3	1	-	1	-	1	-	1	-	1	-	1	-	1	-	0	-

Irritation score is based on Draize Method

[a] Area of opacity not reported; at 24 hours fluorescein test: animal No. 3, corneal staining up to ¼ the surface.

TABLE 2. Summary of Eye Irritation Scores with Time: Conjunctiva and Iris								
Score Conditions	**1 hour**	**24 hours**	**48 hours**	**72 hours**	**4 days**	**5 days**	**6 days**	**7 days**
Conjunctiva								
Erythema	0 to 1	0 to 1	0 to 1	0 to 1	0 to 1	0	0	0
Chemosis	0	0	0	0	0	0	0	0
Discharge	-[a]	-	-	-	-	-	-	-
Iris	0	0	0	0	0	0	0	0

Irritation score is based on Draize Method

[a] Not reported

Scale for Scoring Ocular Lesions

Cornea

A. Opacity-degree of density (area most dense taken for reading)

No ulceration or opacity 0
Scattered or diffuse areas of opacity (other than slight dulling of normal luster), details of iris clearly visible 1
Easily discernible translucent areas, details of iris slightly obscured 2
Nacreous areas, no details of iris visible, size of pupil barely discernible 3
Opaque cornea, iris not discernible through the opacity 4

Iris

A. Values

Normal 0
Marked deepened rugae; congestion; swelling; moderate circumcorneal hyperemia, or injection; iris reactive to light (a sluggish reaction is considered to be an effect) 1
No reaction to light, hemorrhage, gross destruction (any or all of these) 2

Conjunctivae

A. Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)

Normal 0
Some blood vessels hyperemic (injected) 1
Diffuse, crimson color; individual vessels not easily discernible 2
Diffuse beefy red 3

B. Chemosis

Normal 0
Some swelling above normal 1
Obvious swelling with partial eversion of lids 2
Swelling with lids about half closed 3
Swelling with lids more than half closed 4

TABLE 3. Summary of Total[a] and Primary Eye Irritation Scores with Time								
Animal #	1 h	24 h	48 h	72 h	4 d	5 d	6 d	7 d
1	2	0	0	0	0	0	0	0
2	0	2	2	2	0	0	0	0
3	0	7	7	7	7	5	5	0
Average scores[b]	0.7	3.0	3.0	3.0	2.3	1.7	1.7	0.0

[a]Formula: Total Irritation Score = I + II + III, where,
I = Corneal Score = [Density (A) x Area (B)] x 5
II = Iris Score = Severity x 5
III = Conjunctival Score = [Erythema (A) + Chemosis (B) + Discharge (C)] x 2
Under the assumption that the area of opacity was 1/4 and discharge scores were 0.
[b]Average Primary Irritation = Sum of Total Irritation Scores ÷ 3

III. DISCUSSION:

Corneal opacity was noted on 1/3 rabbits at 24 hours after test material instillation with resolution by day 7. Iritis was not noted on any rabbit during the study. No positive conjunctival irritation (score $\geq$ 2) was noted on any rabbit. Some hyperemic blood vessels were noted on animal No. 1 at 60 minutes after test material instillation, on animal No. 2 at 60 minutes through 48 hours, and on animal No. 3 at 24 hours through day 4. The maximum average score was 3.0 at 24, 48, and 72 hours after test material instillation under the assumption that the area of opacity was 1/4 and discharge scores were 0. FeNaEDTA was mildly irritating and is in TOXICITY CATEGORY III. The packet classification is **ACCEPTABLE.**

DATA EVALUATION RECORD

SLUGKIL MP (FENAEDTA)

STUDY TYPE: PRIMARY DERMAL IRRITATION - RABBIT (870.2500)
MRID 47942510

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 10-004

Primary Reviewer:
Susan Chang, M.S.

Signature:
Date: JUN 10 2010

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Signature:
Date: JUN 10 2010

Robert H. Ross, M.S., Group Leader

Signature:
Date: JUN 10 2010

Quality Assurance:
Eric Lewis, M.S.

Signature:
Date: JUN 10 2010

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Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA EVALUATION RECORD

EPA Secondary Reviewer:

STUDY TYPE:	Primary Dermal Irritation - Rabbits (OPPTS 870.2500)
MRID NO:	47942510
DP BARCODE NO:	DP 373965
DECISION NO:	425379
SUBMISSION NO:	866101
TEST MATERIAL:	FeNaEDTA (EPA Reg. No. 67702-GR, ethylenediaminetetraacetic acid iron (III) sodium salt, containing 69.9% EDTA, a.i.)
PROJECT NO:	21620 (Report No.)
SPONSOR:	Neudorff GmbH KG, Postfach 1209, An der Mühle 3, D-31860 Emmerthal, Germany
TESTING FACILITY:	LPT Laboratory of Pharmacology and Toxicology GmbH & Co. KG, P.O. Box 920461, D-21134 Hamburg, Germany
TITLE OF REPORT:	Primary Dermal Irritation
AUTHOR:	Dr. J. Leuschner
STUDY COMPLETED:	August 7, 2007
GOOD LABORATORY PRACTICE:	GLP Compliant, according to EC method B.4. (2004/73/EC) and OECD guideline 404
CONCLUSION:	Very slight erythema was noted on 1/3 rabbits 60 minutes after patch removal with clearance by 24 hours. The primary irritation index was 0.1. FeNaEDTA was essentially non-irritating.
CLASSIFICATION:	ACCEPTABLE -- TOXICITY CATEGORY IV

I. STUDY DESIGN:

1. **Test Material:** FeNaEDTA - ethylenediaminetetraacetic acid iron (III) sodium salt, Batch No. 080 507, containing 69.9% EDTA, a.i.

2. **Test Animals:** Three male young adult Himalayan rabbits were received from LPT Laboratory of Pharmacology and Toxicology GmbH & Co. KG, Branch Löhndorf, 24601 Löhndorf/Post Wankendorf, Germany. The animals were housed individually in cages. The animals were fed commercial diet, ssniff® K-H V 2333 (ssniff Spezialdiäten GmbH, 59494 Soest, Germany). Tap water was available *ad libitum*. The environmental conditions of the animal room were as follows: temperature, 20±3°C; relative humidity, 30-70%; air changes, 60 per hour; and photoperiod, 12 hour light/dark cycle.

3. **Methods:** Rabbits were tattooed (Nos. 1, 2, and 3) and acclimated for at least 20 days. The fur on the dorsal trunk of each rabbit was clipped on the day prior to treatment. One thousand mg of the test material were mixed with 0.5 mL water. The rabbits were treated with 500 mg of test material (= 750 mg of the test mixture) applied to an approximately 6 cm^2 clipped intact dose site, and the site covered with gauze patch. The patch was secured with non-irritating tape. The covering was removed 4 hours later. Dermal examination was recorded at 60 minutes, and 24, 48, and 72 hours after removal of the patch.

II. RESULTS:

1. **Mortality:** All rabbits survived the study.

2. **Dermal responses:** Very slight erythema was noted on 1/3 rabbits 60 minutes after patch removal with clearance by 24 hours. The primary irritation index was 0.1.

Irritation Scores:

TABLE 1. Summary of individual rabbit's dermal irritation scores with time

	Hours			
Animal Nos.	1	24	48	72
1	1/0[a]	0/0	0/0	0/0
2	0/0	0/0	0/0	0/0
3	0/0	0/0	0/0	0/0

Data taken from p. 27, MRID 47942510.
[a]Erythema/Edema

Description of rating method:

Evaluation of Skin Reaction:	**Score**
Erythema formation:	
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation preventing erythema reading	4

Edema Formation:	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised by more than 1 mm extending beyond the area of exposure)	4

III. DISCUSSION:

Very slight erythema was noted on 1/3 rabbits 60 minutes after patch removal with clearance by 24 hours. The primary irritation index was 0.1. FeNaEDTA was essentially non-irritating and is in TOXICITY CATEGORY IV. The packet classification is **ACCEPTABLE.**

DATA EVALUATION RECORD

SLUGKIL MP (FENAEDTA)

STUDY TYPE: SKIN SENSITIZATION (LOCAL LYMPH NODE ASSAY) - MICE (870.2600)
MRID 47942511

Prepared for
Biopesticides and Pollution Prevention Division
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Prepared by
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Task Order No. 10-004

Primary Reviewer:
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Date: JUN 10 2010

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Robert H. Ross, M.S., Group Leader

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Date: JUN 10 2010

Quality Assurance:
Eric Lewis, M.S.

Signature: 
Date: JUN 10 2010

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Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA EVALUATION RECORD

EPA Secondary Reviewer:

STUDY TYPE:	Skin Sensitization (local lymph node assay) - mice (OPPTS 870.2600)
MRID NO:	47942511
DP BARCODE NO:	DP 373965
DECISION NO:	425379
SUBMISSION NO:	866101
TEST MATERIAL:	FeNaEDTA (EPA Reg. No. 67702-GR, ethylenediaminetetraacetic acid iron (III) sodium salt, containing 69.9% EDTA, a.i.)
PROJECT NO:	21622 (Report No.)
SPONSOR:	Neudorff GmbH KG, Postfach 1209, An der Mühle 3, D-31860 Emmerthal, Germany
TESTING FACILITY:	LPT Laboratory of Pharmacology and Toxicology GmbH & Co. KG, P.O. Box 920461, D-21134 Hamburg, Germany
TITLE OF REPORT:	Skin Sensitization
AUTHOR:	Dr. J. Haferkorn
STUDY COMPLETED:	September 27, 2007
GOOD LABORATORY PRACTICE:	GLP Compliant, according to EC method B.42 (2004/73/EC) and OECD guideline 429
CONCLUSION:	No statistically significant increases in lymph node cell counts or ear weights were found in treated mice. The slight increase of the lymph node weight in the test material treated groups was regarded as spontaneous. The positive control produced a dermal sensitization response in mice. FeNaEDTA was not a dermal sensitizer.
CLASSIFICATION:	ACCEPTABLE based on concurrence with OECD TG 429; however, the local lymph node assay procedure "was never validated for mixtures by the assay creators. It is undergoing a validation step through ICCVAM - which is a lead NIEHS group of all gov't agency."

I. STUDY DESIGN:

1. **Test material:** FeNaEDTA - ethylenediaminetetraacetic acid iron (III) sodium salt, Batch No. 080 507, containing 69.9% EDTA, a.i.

2. **Test animals:** Forty-six female CBA/JNCrj mice received from Charles River Laboratories, Research Models and Services, Germany GmbH, Sandhofer Weg 7, 97633 Sulzfeld, Germany were assigned to groups and weighed 20-24 g at experiment start. The young adult animals, approximately 8-10 weeks old, were housed individually in Makrolon cages (type III). The animals were fed commercial diet, ssniff® R/M-H V 1543 (ssniff Spezialdiäten GmbH, 59494 Soest, Germany). Tap water was available *ad libitum*. The environmental conditions of the animal room were as follows: temperature, 22±3°C; relative humidity, 55±15%; air changes, 10 per hour; and photoperiod, 12 hour light/dark cycle.

3. **Methods:** The mice were identified by cage label and grouped: Group 1 [vehicle control; acetone:olive oil (3 + 1, v/v)] – Nos. 1 to 6; Group 2 (10% w/w test material in vehicle) – Nos. 7 to 12; Group 3 (25% w/w test material in vehicle) – Nos. 13 to 18; Group 4 (50% w/w test material in vehicle) – Nos. 19 to 24; Group 6 [positive control; 30% v/v α-hexylcinnamic aldehyde in vehicle) – Nos. P1 to P6. The mice were acclimated for at least five days. The dermal sensitization potential of the test material was examined using the local lymph node assay (LLNA). A preliminary dose-range-finding study was conducted in two animals per dose level (0, 0.5, 1, 2.5, 5, 10, 25, and 50% test material in acetone/olive oil (3+1 v/v)). No sensitizing potential was observed. Hence, the main study concentrations of 10, 25, and 50% w/w test material in acetone/olive oil (3+1 v/v) were used. Body weight was recorded on test day 1 and prior to sacrifice on test day 4. Clinical observations were performed prior to each dose and once daily, and the mice were checked frequently throughout the day. Twenty-five µL of the test material were administered topically to the dorsum of each mouse ear for 3 consecutive days (test days 1 to 3) at 0 [vehicle control: acetone:olive oil (3 + 1, v/v)], 10, 25, and 50% test material in vehicle control; and 30% v/v α-hexylcinnamic aldehyde in vehicle as positive control; respectively. Twenty-four hours after the last application (test day 4), the mice were sacrificed. Ear swelling measurements were carried out at the helical edge of both ears using an Oditest micrometer. Punch biopsies of 8 mm in diameter of the apical area of both ears were prepared and immediately weighed. Lateral pairs of auricular lymph nodes draining the ear tissue were excised, carefully separated from remaining fatty tissue, and weighed immediately following preparation. The lymph nodes were then stored on ice in PBS/0.5% BSA and single cell suspensions prepared by mechanical tissue disaggregation. The cells were counted automatically in a cell counter.

II. RESULTS:

1. **Mortality:** All animals survived the study.

2. **Body Weight:** One mouse in the 50% w/w test material group slightly lost weight. One mouse in the 10% w/w test material group, two mice in the 25% w/w test material group, three mice in the 50% w/w test material group, and five mice in the positive control group did not gain weight.

3. **Clinical signs of Toxicity:** No clinical signs of toxicity were noted in the study.

4. **Stimulation Index Data:** There were no statistically significant increases for the lymph node cell counts and ear weights for the test material treated groups (Table 1). The slight increase

of the lymph node weight in the test material treated groups was regarded as spontaneous, as no statistical significance was noted and the weights obtained were within the normal range observed for control animals. The stimulation indices were calculated by dividing the average lymph node cell counts or ear weights per group of the test material treated animals by the vehicle treated ones. The stimulation indices for the lymph node cell counts were 1.098, 1.170, and 1.045 for 10%, 25%, and 50% test material, respectively. The stimulation indices for the ear weights were 1.037, 1.043, and 1.049 for 10%, 25%, and 50% test material, respectively. The stimulation indices for lymph node cell count, lymph node weight, and ear weight were 1.461, 1.517, and 1.238, respectively, for the positive control. Threshold values of the stimulation indices of lymph node cell count and ear weight were calculated by dividing the average values per group of the test material treated animals by the vehicle treated ones. The stimulation indices for the cell counts above 1.4 or ear weight above 1.1 are considered positive. The positive control produced a dermal sensitization response in mice. FeNaEDTA did not produce a dermal sensitization response in mice and was not a dermal sensitizer.

Table 1 Stimulation Indices[a]

Group	Material tested	No. of animals	Lymph node cell count	Lymph node weight	Ear weight	Difference of ear thickness
1	Vehicle control	6	1.000	1.000	1.000	1.000
2	10% FeNaEDTA	6	1.098	1.034	1.037	1.070
3	25% FeNaEDTA	6	1.170	1.138	1.043	1.113
4	50% FeNaEDTA	6	1.045	1.172	1.049	1.116
6	Positive Control	6	1.461*	1.517*	1.238	1.135

[a] Data taken from p. 21, MRID 47942511.

* Lymph node cell count and lymph node weight significant different from negative control (at $p \leq 0.01$)

III. DISCUSSION:

No statistically significant increases in the indices for the lymph node cell count and ear weight for the test material treated groups were found. The slight increase of the lymph node weight in the test material treated groups was regarded as spontaneous, as no statistical significance was noted and the weights obtained are within the normal range observed for control animals. The stimulation indices for the lymph node cell counts were 1.098, 1.170, and 1.045 for 10%, 25%, and 50% test material, respectively. The stimulation indices for the ear weights were 1.037, 1.043, and 1.049 for 10%, 25%, and 50% test material, respectively. The stimulation indices for the lymph node cell count, lymph node weight, and ear weight were 1.461, 1.517, and 1.238, respectively, for the positive control. FeNaEDTA was not a dermal sensitizer. The present study does not meet the guideline requirements of OPPTS 870.2600, but was compliant with OECD TG 429 (2002). The packet is classified as **ACCEPTABLE,** although the local lymph node assay procedure "was never validated for mixtures by the assay creators. It is undergoing a validation step through ICCVAM - which is a lead NIEHS group of all gov't agency."

DATA EVALUATION RECORD

SLUGKIL MP (FENAEDTA)

STUDY TYPE: ACUTE INHALATION TOXICITY - RAT (870.1300)
MRID 47942512

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 10-004

Primary Reviewer:
Susan Chang, M.S.

Signature:
Date: JUN 10 2010

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Signature:
Date: JUN 10 2010

Robert H. Ross, M.S., Group Leader

Signature:
Date: JUN 10 2010

Quality Assurance:
Eric Lewis, M.S.

Signature:
Date: JUN 10 2010

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA EVALUATION RECORD

EPA Secondary Reviewer:

STUDY TYPE:	Acute Inhalation Toxicity - Rats (OPPTS 870.1300)
MRID NO:	47942512
DP BARCODE NO:	DP 373965
DECISION NO:	425379
SUBMISSION NO:	866101
TEST MATERIAL:	FeNaEDTA (EPA Reg. No. 67702-GR, ethylenediaminetetraacetic acid iron (III) sodium salt, containing 69.9% EDTA, a.i.)
PROJECT NO:	21619 (Report No.)
SPONSOR:	Neudorff GmbH KG, Postfach 1209, An der Mühle 3, D-31860 Emmerthal, Germany
TESTING FACILITY:	LPT Laboratory of Pharmacology and Toxicology GmbH & Co. KG, P.O. Box 920461, D-21134 Hamburg, Germany
TITLE OF REPORT:	Inhalation
AUTHOR:	Dr. J. Haferkorn
STUDY COMPLETED:	January 8, 2008
GOOD LABORATORY PRACTICE:	GLP Compliant, according to EC method B.2 (92/69/EEC) and OECD guideline 403
CONCLUSION:	The inhalation LC_{50} for males, females, and combined sexes was > 2.75 mg/L.
CLASSIFICATION:	ACCEPTABLE -- TOXICITY CATEGORY IV

I. STUDY DESIGN:

1. **Test Material:** FeNaEDTA - ethylenediaminetetraacetic acid iron (III) sodium salt, Batch No. 080 507, containing 69.9% EDTA, a.i.

2. **Test Animals:** Five male and five female CD/Crl:CD(SD) rats were received from Charles River Laboratories, Research Models and Services, Germany GmbH, Sandhofer Weg 7, 97633 Sulzfeld, Germany and weighed 228-250 g (males) and 214-241 g (females) on the day of exposure. The young adult animals, 51-65 days old, were housed in groups of 2-3 per sex in Makrolon cages (type III). The animals were fed commercial diet, ssniff® R/M-H V 1534 (ssniff Spezialdiäten GmbH, 59494 Soest, Germany). Drinking water in bottles was available *ad libitum*. The environmental conditions of the animal room were as follows: temperature, 22±3°C; relative humidity, 55±15%; and air changes, 12-18 per hour; photoperiod, 12 hour light/dark cycle.

3. **Methods:** Rats were identified by colored marks and cage labels: Male – Nos. 1m to 5m; Female – Nos. 6f to 10f. The rats were acclimated for at least 5 days prior to exposure. The animals were exposed to the concentration shown in Table 1. The test material was dissolved in water as a 5.7% solution (approximately limit of solubility). The rats were exposed nose-only in a dynamic flow inhalation chamber for four hours. The animals were observed at 0, 5, 15, 30, and 60 minutes, and 3 hours after exposure and at least once daily thereafter for 14 days. They were weighed prior to test material exposure and on test days 8 and 15. All rats were sacrificed and necropsied at the end of the study.

TABLE 1. Concentrations, exposure conditions, mortality/animals treated

Nominal Conc. (µL/L)	Grav. Conc. (mg/L)	MMAD (µm)	GSD (µm)	Particles ≤4 µm (%)	Temp (°C)	Humidity (%)	Mortality		
							Male	Female	Combined
55.56	2.75	2.730	5.20	44.1	20.9-22.0	Not reported	0/5	0/5	0/10

Data taken from pp. 22, 24, 28, 29, 30, and 31, MRID 47942512.

Generation of the test atmosphere and description of the chamber: Prior to aerosolization, the test material was dissolved in water to a 5.7% solution (approximately limit of solubility). The exposure atmosphere was generated using a spray-jet (Type 970, Düsen-Schlick GmbH, 96253 Untersiemau, Germany). The spay-jet was fed with compressed air at 5.0 bar from a compressor and with the test material using an infusion pump. The oxygen content in the chamber was 21%. The air flow entrance and flow exit were 900 and 800 L/h, respectively, to produce a homogenous distribution and a positive pressure in the chamber. There were 22.5 air changes per hour. The nose-only cylindrical exposure chamber volume was 40 L with an equilibration time of 15 min.

Test atmosphere concentration: During exposure, gravimetric samples were collected using an air sample filter from the breathing zone of the animals once every hour during exposure. Filters were weighed before and after sampling. Before weighing the filters were

dried for 30 minutes at 100°C. The nominal and the actual concentrations were reported, but no explanations of calculation were given.

Particle size determination: Particle size for exposure concentration was determined twice using an eight-stage cascade impactor. The test material concentration collected at each stage was determined gravimetrically. The mass median aerodynamic diameter was estimated by means of non-linear regression analysis. The geometric standard deviation was calculated from the quotient of the 84%- and the 50%-mass fractions, obtained from the non-linear regression analysis. Result are in Table 1 above.

II. RESULTS:

1. **Mortality:** All rats survived the study.

2. **Clinical Observations:** No signs of toxicity were noted during the study.

3. **Body Weight:** All rats gained weight during the study.

4. **Gross Necropsy:** No pathological findings were noted at necropsy.

III. DISCUSSION:

The inhalation LC_{50} for males, females, and combined sexes was > 2.75 mg/L. This places FeNaEDTA in TOXICITY CATEGORY IV. The packet classification is **ACCEPTABLE.**

DATA EVALUATION RECORD

SODIUM FERRIC EDTA
(Slugkil MP)

STUDY TYPE: Summary of Published Toxicology Data (Nonguideline)

MRID 47942517

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
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Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
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Oak Ridge, TN 37830
Task Order No. 10-004

Primary Reviewer:
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Date: JUN 10 2010

Quality Assurance:
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Signature: L. A. Wilson
Date: JUN 10 2010

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA EVALUATION RECORD

EPA Secondary Reviewer:	
STUDY TYPE:	Summary of Published Toxicology Data (Nonguideline)
MRID NO:	47942517
DECISION NO:	425379
DP BARCODE:	DP373965
TEST MATERIAL:	Slugkil MP (a.i., 71.42% w/w sodium ferric EDTA)
PROJECT STUDY NO:	None
SPONSOR:	W. Neudorff GmbH KG, An der Muhle 3, 31860 Emmerthal, Germany
TESTING FACILITY:	Not appplicable
TITLE OF REPORT:	Compilation of Toxicology Data
AUTHOR:	Talerek, W.G.
STUDY COMPLETED:	November 30, 2009
CONFIDENTIALITY CLAIMS:	None.
GOOD LABORATORY PRACTICE:	A signed and dated GLP statement was included. The submitter was neither the sponsor of the study nor conducted it, and does not know if it was conducted in accordance with 40 CFR Part 160.
CONCLUSION:	The information provided indicates that the components of sodium ferric EDTA are not likely to produce adverse toxic effects at exposure levels expected from the recommended use of the product. However, a conclusion for sodium ferric EDTA itself cannot be drawn.
CLASSIFICATION:	Supplemental.

CONTAINS CONFIDENTIAL BUSINESS INFORMATION

Introduction

Slugkil MP is a manufacturing use product to be used to formulate end use product molluscicides intended for home and garden, commercial, and agricultural use. The active ingredient in the product is 71.42% w/w sodium ferric EDTA. The inert ingredient is [redacted].

MRID 47942517 is a compilation of published literature related to the toxicology of the components of sodium ferric EDTA. Relevant portions of each of the publications are summarized below.

Summary of Literature

Candela, E., M.V. Camacho, C. Martinez-Torres, et al. 1984. Iron Absorption by Humans and Swine from Fe(III)-EDTA. Further Studies. J. Nutr. 114:2204-2211.

Six human subjects drank a solution containing 5 mg of Fe as Fe(III)-EDTA labeled with ^{59}Fe. Urine was collected over 48 hours, and blood was drawn 15 days later. Mean iron absorption was 12.0%, and elimination via urine was 0.3%. The greatest amount of iron eliminated in the urine occurred during the first 24 hours.

Sixteen male pigs were fed a commercial feed containing $Na^{55}Fe$-[2-^{14}C]EDTA and maintained in metabolic cages. About 5% of the ^{55}Fe was absorbed from the pylorus and upper jejunum and transferred very slowly to the plasma, where it was incorporated into the hemoglobin. Less than 1% was excreted by the kidneys. The remainder was excreted in the feces, mostly in an insoluble form. About 5% of the administered ^{14}C was absorbed in the duodenum and jejunum, transferred to the plasma, and excreted by the kidneys. The remainder was excreted in the feces, about 80% in a soluble form.

Dunkel, V.C., R.H.C. San, H. E. Seifried, et al. 1999. Genotoxicity of Iron Compounds in *Salmonella typhimurium* and L5178Y Mouse Lymphoma Cells.

NaFeEDTA was positive for mutagenicity in the L5178Y TK +/- Mouse Lymphoma Assay in both the absence and presence of S9. The range of test concentrations was 1.3-325 µg Fe/mL without S9 and 0.26-6.5 µg Fe/mL with S9.

Gasset, A.R. and T. Akaboshi. 1977. Embryopathic Effect of Ophthalmic EDTA. Invest. Ophthalmol. Visual Sci. 16(7):652-654.

Pregnant adult albino rabbits received two drops of 0.1% or 3.0% EDTA solution in each eye six times per day from the sixth to the eighteenth day of gestation. On gestation day 29, they were sacrificed and the fetuses were removed for external and histological examination. Although no teratological effect was found at either dose, the 3.0% dose produced an embryopathic effect, with only 30% of the progeny classified as normal.

Heimbach, J., S. Rieth, F. Mohamedshah, et al. 2000. Safety Assessment of Iron EDTA [Sodium Iron (Fe^{3+}) Ethylenediaminetetraacetic Acid]: Summary of Toxicological, Fortification, and Exposure Data. Food and Chemical Toxicology 38:99-111.

Iron EDTA dissociates in the gastrointestinal tract to iron and an EDTA salt, each of which is absorbed independently. The available evidence suggests that normal individuals are able to control the absorption of iron despite high intakes. EDTA compounds are poorly absorbed from the gastrointestinal tract and have a low acute oral toxicity. They have not been found to have reproductive or developmental toxicity when administered orally along with nutritionally adequate diets. In chronic toxicity studies, no adverse effects were seen at 5% EDTA in the diet. EDTA compounds have not been found to be carcinogenic or directly genotoxic. Historical data demonstrate that iron EDTA is safe and effective when used to fortify food products, and meets the standard of "reasonable certainty of no harm."

The authors note that the positive result for mutagenicity for NaFeEDTA found in the mouse lymphoma test by Dunkel et al. (1999) described above most likely reflected the sensitivity of the L5187Y cells to abnormal iron concentrations, and conclude that EDTA-metal complexes lack significant genotoxic potential.

Kimmel, C.A. 1977. Effect of Route of Administration on the Toxicity and Teratogenicity of EDTA in the Rat. Toxicology and Applied Pharmacology 40:299-306.

The toxic and teratogenic effects of EDTA in rats were determined after it was administered either in the diet (954 mg/kg/day), by gastric intubation (625 mg/kg twice a day or 750 mg/kg twice a day), or subcutaneously (375 mg/kg). The treatments were applied on gestation days 7 through 14 and the animals were sacrificed on gestation day 21. EDTA in the diet produced severe maternal toxicity and malformations in 71% of the offspring. EDTA by intubation resulted in 36% maternal death at 625 mg/kg twice daily and 87.5% maternal death at 750 mg/kg twice daily. At 625 mg/kg twice daily, the malformation rate was 20.5%. The subcutaneous route produced 24% lethality in dams and 4.3% malformations in the offspring.

McGregor, D.B., A. Brown, P. Cattanach, et al. 1988. Responses of the L5178Y tk^+/tk^- Mouse Lymphoma Cell Forward Mutation Assay: III. 72 Coded Chemicals. Environmental and Molecular Mutagenesis 12:85-154.

EDTA, trisodium salt, at concentrations up to 5000 µg/mL did not produce mutagenic responses with or without added S9.

National Cancer Institute. 1977. Bioassay of Trisodium Ethylenediaminetetraacetate Trihydrate (EDTA) for Possible Carcinogenicity. DHEW Publication No. 77-811. NTIS, Springfield,VA.

Concentrations of 3750 or 7500 ppm $Na_3EDTA\text{-}3H_2O$ were administered in the diet to Fischer 344 rats and B5C3F1 mice for 103 weeks. There were no treatment-related signs of clinical toxicity, and mortality was similar among the treatment and control groups. The test material produced no evidence of carcinogenicity in this study.

Oser, B.L., M. Oser, and H.C. Spencer. 1963. Safety Evaluation Studies of Calcium EDTA. Toxicology and Applied Pharmacology 5:142-162.

CaEDTA (50, 125, or 250 mg/kg body weight) was fed in the diet to groups of male and female Wistar rats for up to two years. After approximately 13 weeks, the rats were mated and the offspring were raised on their respective parents' diets. This was repeated for two additional generations. There were no adverse effects on growth, food efficiency, or hematology parameters on the F_0 generation or the three succeeding generations maintained on the same diet. There were no adverse effects on reproduction or lactation efficiency, and no treatment-related gross or microscopic findings.

Additionally, groups of mongrel dogs were administered diets containing 50, 100, or 250 mg CaEDTA/kg body weight for up to one year. All dogs survived and gained weight. There were no significant deviations from control values for urine or blood chemistry parameters. Gross and histopathologic results were unremarkable.

Swenerton, H. and L.S. Hurley. 1971. Teratogenic Effects of a Chelating Agent and Their Prevention by Zinc. Science 173:62-63.

A diet containing 3% EDTA fed to groups of female Sprague-Dawley rats during gestation days 6-21 produced gross congenital malformations in all the full-term young. These effects were prevented by supplementing the 3% EDTA diet with 1000 ppm zinc during gestation days 6-21.

World Health Organization. 2005. Sodium Iron EDTA. WHO Food Additives Series 32.

The Joint FAO/WHO Expert Committee on Food Additives (JEFCA) provisionally concluded that use of sodium iron EDTA in supervised food fortification programs in iron-deficient populations does not present a safety problem. The Committee requested that additional studies be conducted to assess the deposition site of iron administered in this form and to assess the metabolic fate of sodium iron EDTA following long-term administration.

World Health Organization. 2000. Sodium Iron Ethylenediamine Tetraacetic Acid (EDTA). WHO Food Additives Series 4.

JEFCA concluded that sodium iron EDTA could be considered safe for use in supervised food fortification programs when public officials had determined the need for iron supplementation of the diet of a population. Such programs would provide a daily iron intake of approximately 0.2 mg/kg body weight.

Anonymous. 1964. Toxicology of EDTA. Food and Cosmetics Toxicology 2:763-767.

Summary of the thesis, "Toxicological Investigation of Ethylenediaminetetraacetic Acid in the Rat." S-S. Yang. 1952.

A single oral dose of Na_2EDTA in rats produced an LD_{50} of 2.0-2.2 g/kg body weight.

A challenge injection of 0.1 mL of 0.1% Na_2EDTA did not produce an allergic response in guinea pigs two weeks after a series of 10 injections given on alternate days.

There were no deaths in albino rats fed 0.5, 1.0, or 5.0% Na_2EDTA in the diet for 12 weeks. The high-dose group consisted of littermates born of an animal that had been fed a diet containing 0.5% EDTA for eight months. There were no toxic effects, except that the high-dose group suffered continuous diarrhea and consumed less food than the other groups. The test continued for a total time of two years, after which there were no treatment-related changes in growth, food consumption, hematology, or mortality. There were no adverse or gross or microscopic findings.

A separate group of rats on a mineral-deficient diet was fed 0.5 or 1.5% Na_2EDTA or 1.5% $Na_2CaEDTA$ for four months. There was no mortality and all groups exhibited a similar general condition.

Summary of thesis, "Some Toxicological and Physiological Studies of Ethylenediaminetetraacetic Acid in the Albino Rat." M.S. Chan. 1956.

Albino rats on the same mineral-deficient diet as in the Yang study were fed 0.5 or 1.0% Na_2EDTA or 0.1 or 1.0% $Na_2CaEDTA$ for 205 days. Growth of males receiving 1.0% Na_2EDTA and females receiving 1.0% $Na_2CaEDTA$ was retarded. Diarrhea and anemic appearance were noted in the 1.0% Na_2EDTA group. This group also had significantly higher blood coagulation

time, higher blood serum calcium values, and increased dental erosion. There were no appreciable differences at gross or microscopic examination.

In a biochemical study, weanling and adult rats were intubated and administered oral doses equivalent to the 1% dietary levels of Na_2EDTA or $Na_2CaEDTA$. After 48 hours, almost all EDTA was eliminated from the body, mostly (>85%) in the feces. After a single oral dose of 95 mg Na_2EDTA, 93% was recovered in the colon after 32 hours.

Study Author's Conclusions

The study author made no conclusions.

Reviewer's Comments

Most of the information provided was for the individual components of sodium ferric EDTA, not for the compound itself. Generally, the information provided indicates that the components of sodium ferric EDTA are not likely to produce adverse toxic effects at exposure levels expected from the recommended use of the product. However, a conclusion for sodium ferric EDTA itself cannot be drawn.

DATA EVALUATION RECORD

SODIUM FERRIC EDTA
(Slugkil MP)

STUDY TYPE: Summary of Published Environmental Fate Data
(Nonguideline)

MRID 47942518

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
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Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37830
Task Order No. 10-004

Primary Reviewer:
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Quality Assurance:
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Date: JUN 10 2010

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA EVALUATION RECORD

EPA Secondary Reviewer:	
STUDY TYPE:	Summary of Published Environmental Fate Literature (Nonguideline)
MRID NO:	47942518
DECISION NO:	425379
DP BARCODE:	DP373965
TEST MATERIAL:	Slugkil MP (a.i., 71.42% w/w sodium ferric EDTA)
PROJECT STUDY NO:	None
SPONSOR:	W. Neudorff GmbH KG, An der Muhle 3, 31860 Emmerthal, Germany
TESTING FACILITY:	Not appplicable
TITLE OF REPORT:	Compilation of Environmental Fate Data
AUTHOR:	Talerek, W.G.
STUDY COMPLETED:	November 30, 2009
CONFIDENTIALITY CLAIMS:	None.
GOOD LABORATORY PRACTICE:	A signed and dated GLP statement was included. The submitter was neither the sponsor of the study nor conducted it, and does not know if it was conducted in accordance with 40 CFR Part 160.
CONCLUSION:	The information provided indicates that sodium ferric EDTA would likely be slowly degraded by photolysis and/or naturally-occurring microorganisms in surface waters and by naturally-occurring microorganisms in agricultural soils.
CLASSIFICATION:	Supplemental.

CONTAINS CONFIDENTIAL BUSINESS INFORMATION

Introduction

Slugkil MP is a manufacturing use product to be used to formulate end use product molluscicides intended for home and garden, commercial, and agricultural use. The active ingredient in the product is 71.42% w/w sodium ferric EDTA. The inert ingredient is [redacted].

MRID 47942518 is a compilation of published literature related to the environmental fate of components of sodium ferric EDTA. Relevant portions of each of the publications are summarized below.

Summary of Literature

Belly, R.T., J.J. Lauff, and C.T. Goodhue. 1975. Degradation of Ethylenediaminetetraacetic Acid by Microbial Populations from an Aerated Lagoon. Applied Microbiology 29(6):787-794.

This paper reports microbial degradation of the sodium- or ammonium-ferric chelate of EDTA (Na- or NH_4Fe-EDTA) by mixed populations of microorganisms present in an aerated industrial lagoon. A radiorespirometric technique showed that 27% of the acetate-2-C and 31% of the ethylene position of the ammonium ferric chelate of ^{14}C-EDTA were recovered as $^{14}CO_2$ after

five days of incubation. In a separate test using the sodium ferric chelate, gas liquid chromatography and total organic carbon analyses showed 89% and 63% reductions of EDTA, respectively, over a similar period. $^{14}CO_2$ evolution was strongly inhibited by heat treatment of the samples or by the addition of antibiotics to the incubation mixtures. Possible intermediates of EDTA degradation were identified using mass spectral analysis.

Bucheli-Witschel, M. and T. Egli. 2001. Environmental Fate and Microbial Degradation of Aminopolycarboxylic Acids. FEMS Microbioloy Reviews 25:69-106.

Biodegradation is apparently of minor importance for EDTA in the environment. Thermic hydrolysis and indirect photolysis have negligible effects. Direct photodegradation of iron (III)-complexed EDTA appears to be mostly responsible for its elimination. Reported half-lives in surface waters ranged from 11.3 minutes to >100 hours. Negligible adsorption has been reported for EDTA on humic acids, silica, kaolin, river sediments, humus solids, and activated sludge particles. While reports have described biologically-mediated degradation of EDTA under laboratory conditions, there has been no indication for significant elimination in municipal wastewater treatment plants. Reports of EDTA degradation in soils and sediments have been contradictory. Successful isolation of EDTA-degrading bacteria, including *Agrobacterium radiobacter* and *Mesorhizobium loti*, has been reported.

Dyanand, S. and M.K. Sinha. 1979. Kinetics of FeEDTA Reactions in Calcareous Soils. Soil Science 127(4):202-210.

In a laboratory test, kinetics of the reaction of FeEDTA with seven soils having a wide range of $CaCO_3$ content (0-22%) was studied. During the first 2-72 hours, the reaction followed first-order kinetics. When FeEDTA reacted with the soils, the EDTA ligands formed complexes with other cations in the soil solution. CaEDTA was initially the dominant species formed, while ZnEDTA and CuEDTA also formed as the reaction time increased.

Frank, R. and H. Rau. 1990. Photochemical Transformation in Aqueous Solution and Possible Environmental Fate of Ethylenediaminetetraacetic Acid (EDTA). Ecotoxicology and Environmental Safety 19:55-63.

Since EDTA is not volatile, it is released into the environment mainly via wastewater. In wastewater treatment plants, EDTA is not transformed by microorganisms or adsorbed to sewage sludge. It is believed that most of the EDTA in surface waters is present in the form of Fe(III) complexes. The removal of EDTA from surface waters can occur via photochemical reactions of the FeEDTA complex. Using optical absorption coefficients of the FeEDTA spectrum at pH 7, quantum yields at pH 7, and an oxygen content near the air-saturated value, the mean half-life of FeEDTA in the Neckar River in Germany was estimated to range from 5 to 480 hours. Degradation of the FeEDTA was fastest during the summer months. Other abiotic transformation processes for FeEDTA could be reactions with OH radicals and singlet oxygen, but these processes are likely to be minor.

FeL^- and CaL^{2-} are again the predominant complexes at low and high pH, but ZnL^{2-} becomes the major complex between pH 6 and 7.

Lockhart, Jr., H.B. and R.V. Blakeley. 1975. Aerobic Photodegradation of Fe(III)-(Ethylenedinitrilo)Tetraacetate (Ferric EDTA). Environ. Sci. Technol. 9:1035-1038.

Photodegradation of aqueous solutions of ferric-1-^{14}C-EDTA at pH 4.5, 6.9, and 8.5 was investigated under irradiation from a wide-spectrum xenon arc lamp. The rate of photodegradation was pH-dependent, and was most rapid at pH 4.5. At a light intensity of 4000 foot candles and an initial Fe(III)-EDTA concentration of 0.0016M, EDTA was completely removed after 24 hours of irradiation at pH 4.5 or 6.9, and after 32 hours at pH 8.5. Major photodegradation products included carbon dioxide, formaldehyde, N-carboxy-methyl N,N'-ethylenediglycine (ED3A), N,N'-ethylenediglycine (EDDA-N,N'), iminodiacetic acid (IMDA), N-carboxymethyl-N-aminoethyleneglycine (EDDA-N,N'), N-aminoethyleneglycine (EDMA), and glycine.

Metsarinne, S., T. Tuhkanen, and R. Aksela. 2001. Photodegradation of Ethylenediaminetetraacetic Acid (EDTA) and Ethylenedaimine Disuccinic Acid (EDDS) within Natural UV Radiation Range. Chemosphere 45:949-955.

Photodegradation of Fe(III)-EDTA and Fe(III)-EDDS in humic lake water or distilled water exposed to sunlight or artificial light (UV radiation at 315-400 nm) was investigated at an initial pH of 3.1 or 6.5. Under artificial light at pH 3.1, the half life of Fe(III)-EDTA was 14.0 minutes in distilled water and 31.1 minutes in lake water. At pH 6.5, the half life was 45.0 minutes in distilled water and 56.8 minutes in lake water. Under sunlight at pH 6.5, Fe(III)-EDTA degraded completely after one week in either distilled or lake water. At pH 3.1, it degraded completely after one day in distilled water and two days in lake water.

Svenson, A., L. Kaj, and H. Bjorndal. 1989. Aqueous Photolysis of the Iron (III) Complexes of NTA, EDTA and DTPA. Chemosphere 18(9/10):1805-1808.

A ferric EDTA solution was illuminated in a Xenotest 1200 apparatus with a sun spectrum representing daily and yearly maxima at 60°N latitude. The calculated half life in the top millimeters of a body of water in Stockholm under optimum degradation conditions was 42.9 minutes.

Sykora, V., P. Pitter, I. Bittnerova, et al. 2001. Biodegradabilitiy of Ethylenediamine-Based Complexing Agents. Wat. Res. 35(8):2010-2016.

Biodegradation of ethylenediamine derivatives with different kinds and number of substituents were conducted. Initial concentrations of complexing agents were about 100 mg/L, corresponding to 0.34 mmol/L EDTA. The inoculum was either non-adapted or activated sewage sludge from a municipal water treatment plant in Prague. EDTA was among the most stable compounds.

Kari, F.G., S. Hilger, and S. Canonica. 1995. Determination of the Reaction Quantum Yield for the Photochemical Degradation of Fe(III)-EDTA: Implications for the Environmental Fate of EDTA in Surface Waters. Environmental Science & Technology 29(4):1008-1017.

The photochemical reaction quantum yield of Fe(III)EDTA at concentrations <1 μM was determined as a function of wavelength, pH, and temperature. The quantum yield was not influenced by pH, was slightly influenced by temperature, and strongly influenced by wavelength. At wavelengths of 313, 366, and 405 nm (at 25°C), the average quantum yields were 0.082, 0.034, and 0.018, respectively. The quantum yields were used to predict typical photochemical half-lives of Fe(III)EDTA in the Glatt River, Switzerland. The predicted half lives at the water surface ranged from about 15 minutes in June to about 140 minutes in December.

Kunkely, H. and A. Vogler. 1994. Photochemistry of the Oxo-Bridge Diiron(III)Core. Evolution of Oxygen Induced by FE^{III} to Fe^{III} Charge-Transfer Excitation of μ-Oxobis[(Ethylenediaminetetraacetato)Ferrate(III)]. J. Chem. Soc., Chem. Commun.: 2671-2672.

The reversible photolysis of aqueous $[\{Fe^{III}(EDTA)\}_2O]^{4-}$ leads to the evolution of oxygen and the formation of $[Fe^{II}(EDTA)]^{2-}$. This paper suggests that the photoreaction is induced by Fe^{III} to Fe^{III} charge-transfer excitation, which yields Fe^{II} and Fe^{IV}=O in the primary photochemical step.

Lahav, N. and M. Hochberg. 1975. Kinetics of Fixation of Iron and Zinc Applied as FeEDTA, FeEDDHA and ZnEDTA in the Soil. Soil. Sci. Soc. Amer. Proc. 39: 55-58.

In column tests using Rehovot sand, pH 7.1-7.2, the fixation of iron applied as FeEDTA was a first-order reaction. FeEDDHA was not adsorbed, and adsorption of ZnEDTA was negligible.

Lauff, J.J., D. B. Steele, L.A. Coogan, et al. 1990. Degradation of the Ferric Chelate of EDTA by a Pure Culture of an *Agrobacterium* sp. Applied and Experimental Microbiology 56(11):3346-3353.

A pure culture of an *Agrobacterium* that mineralizes ferric-EDTA was isolated and grown on ferric-EDTA as the sole carbon source at concentrations >100 mM. As degradation proceeded, carbon dioxide, ammonia, and an unidentified metabolite(s) were produced, the pH increased, and iron precipitated from solution. When sodium ferric EDTA was the substrate, the maximum degradation rate was 24 mM/day. At a substrate concentration of 35 mM, 90% was degraded in three days. Less than 15% of the initial carbon present was incorporated into the cell mass.

Lindsay, W.L. and W.A. Norvell. 1969. Equilibrium Relationships of Zn^{2+}, Fe^{3+}, Ca^{2+}, and H^+ with EDTA and DTPA in Soils. Soil Sci. Soc. Amer. Proc. 33:62-68.

Mole-fraction diagrams were derived for EDTA and DTPA in soils when the competing cations are either Fe^{3+}, Ca^{2+}, and H^+, or Zn^{2+}, Fe^{3+}, Ca^{2+}, and H^+. When the competing cations are Fe^{3+}, Ca^{2+}, and H^+, the major metal complex is FeL^- (where L^- is the free ligand) below pH 6.8 and CaL^{2-} above pH 6.8. The $Fe(OH)L^{2-}$ complex reaches 0.05 mole fraction at pH 6.6 but decreases at both higher and lower pH values. The $FeHL$, $CaHL^-$, and $Fe(OH)_2L^{3-}$ complexes are of less significance in the range of pH 4 to 9. When the competing metals are Zn^{2+}, Fe^{3+}, Ca^{2+}, and H^+,

Thomas, R.A.P., K. Lawlor, M. Bailey, et al. 1998. Biodegradation of Metal-EDTA Complexes by an Enriched Microbial Population. Applied and Environmental Microbiology 64(4):1319-1322.

A mixed culture of microorganisms isolated from samples of River Mersey (UK) water and industrial effluent treatment plant sludge was provided with EDTA as the sole carbon source for 30 days. Organisms included represented *Methylobacterium*, *Variovorax*, *Enterobacter*, *Aureobacterium*, and *Bacillus*. The culture slowly biodegraded metal-EDTA complexes in the order Fe >Cu >Co >Ni >Cd.

Tiedje, J.M. 1975. Microbial Degradation of Ethylenediaminetetraacetate in Soils and Sediments. Applied Microbiology 30(2):327-329.

Agricultural soil and lake sediment samples were incubated under aerobic conditions in flasks with ^{14}C-EDTA (4.0 µg free acid/g soil) or mixed culture medium containing 4.5 µg ^{14}C-EDTA/mL of mineral salts. EDTA chelates of Cu, Cd, Zn, Mn, Ca, and Fe added to the soil were equally degraded; Ni-EDTA was degraded more slowly. Results were similar for the sediment tests.

Tiedje, J.M. 1977. Influence of Environmental Parameters on EDTA Biodegradation in Soils and Sediments. J. Environ. Qual. 6(1):21-26.

Agricultural soil samples representing different origins, textures, uses, and pH were incubated with ^{14}C-labelled EDTA (generally 2.5-4.5 ppm µg free acid/g soil) under aerobic or anaerobic conditions. Sediments from the Detroit River-Lake Erie area were also included in the tests. All the soils and sediment tested slowly degraded the ^{14}C-EDTA to $^{14}CO_2$ under aerobic conditions, but no $^{14}CO^2$ was produced under anaerobic conditions. Degradation appeared to result from co-metabolism by established microbial populations. Degradation was seen up to 1000 ppm EDTA, the highest concentration tested. Soil samples collected in winter produced more than twice the degradation than those collected in summer.

Hill-Cottingham, D.G. and C.P. Lloyd-Jones. 1961. Absorption and Breakdown of Iron-Ethylenediamine Tetraacetic Acid by Tomato Plants. Nature 169:312.

Tomatoes grown in iron-free nutrient solution were transferred to nutrient solution containing 1 ppm iron as FeEDTA. The iron was labeled with Fe-59 and the EDTA with C-14. The plants and nutrient solution were analyzed after 10, 17, and 24 days. After 10 days, 41% of the added iron and 26% of the C-14 were recovered in the plants. After 24 days, nearly all the added iron was recovered from the plants or solutions; recovery of C-14 was about 60%, indicating decomposition of the EDTA.

Study Author's Conclusions

The study author made no conclusions.

Reviewer's Comments

The information provided indicates that sodium ferric EDTA would likely be slowly degraded by naturally-occurring microorganisms in surface waters and agricultural soils.